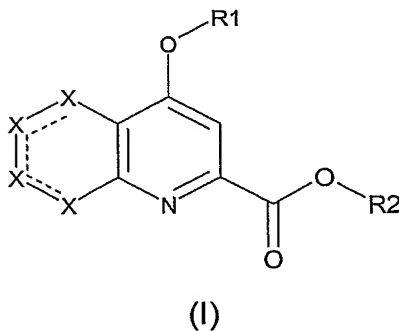


CLAIMS

1. Use of a derivative of the general formula (I) for the preparation of a medicament for the prevention of and/or treating hyperglycaemia-related pathologies:



in which:

X represents, independently of each other,

- a carbon atom, optionally substituted by a group chosen from: alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, alkylaryl, heteroaryl, -CN, halogen, -O-aryl, -O-heteroaryl, cycloalkyl, heterocyclyl, -CO₂H, -C(=O)-alkyl, -C(=O)-aryl, -C(=O)-cycloalkyl, -C(=O)O-alkyl, -C(=O)NRR', -OH, -O-alkyl, -O-alkylaryl, -C(=O)O-aryl, -NRR', -S(O)_pR, in which p represents 0, 1 or 2, or two adjacent carbon atoms may form an aromatic ring fused to the aryl nucleus, or
- a nitrogen, oxygen or sulfur atom;

R1 and R2, which may be identical or different, independently represent a group chosen from:

- Hydrogen,
- alkyl, alkenyl, alkynyl, each optionally and independently substituted by one or more of the following groups: -CN, halogen, aryl, biaryl, -O-aryl, -O-heteroaryl, -O-heterocycloalkyl, cycloalkyl, heterocycloalkyl, -CO₂H, -C(=O)-alkyl, -C(=O)-aryl, -C(=O)-cycloalkyl, -C(=O)O-alkyl, -C(=O)NRR', -OH, -O-alkyl, -O-alkylaryl, -C(=O)O-aryl, -NRR', -S(O)_pR, in which p represents 0, 1 or 2;

in which:

aryl is optionally and independently substituted by one or more groups chosen from: -CN, halogen, aryl, alkyl, -O-alkyl, -alkyl-C(=O)O-alkyl, -alkyl-C(=O)OH, -O-

alkylaryl, heterocycloalkyl, -NRR', -OH, -S(O)_pR, in which p represents 0, 1 or 2; -O-aryl, perhaloalkyl, -COOH, COOR;


heteroaryl is optionally and independently substituted by one or more groups chosen from halogen, -COOH, -COOR and heterocycloalkyl;

5 heterocycloalkyl is optionally and independently substituted by one or more alkyl or = O;

- cycloalkyl or heterocycloalkyl, each optionally and independently substituted by alkyl or alkoxy;

- aryl or heteroaryl, each optionally and independently substituted by one or
10 more groups chosen from -CN, halogen, aryl, alkyl, -O-alkyl, -alkyl-C(=O)O-alkyl, -O-alkylaryl, heterocycloalkyl; -NRR', -OH, -S(O)_pR, in which p represents 0, 1 or 2; -O-aryl, perhaloalkyl, -COOH, COOR;

R and R' are chosen from H and alkyl;

15  represents a single bond or a double bond;

and also the tautomeric forms, enantiomers, diastereoisomers and epimers, and the pharmaceutically acceptable salts.

2. Use according to Claim 1, for which, in formula (I), each of the X repre-
20 sents a carbon atom, optionally substituted by a halogen atom.

3. Use according to Claim 1 or 2, in which the carbon in position 6 of the quinoline ring is substituted by a halogen atom.

25 4. Use according to any one of the preceding claims, for which the halogen substituent of X is a fluorine atom.

5. Use according to any one of the preceding claims, for which R1 and/or R2 independently represent(s) a hydrogen atom, alkyl, alkenyl, alkynyl, optionally
30 substituted by -CN, halogen, -O-aryl, -O-heteroaryl, cycloalkyl, heterocycloalkyl, -COOH, -C(=O)-aryl, -C(=O)-cycloalkyl, -C(=O)O-alkyl, -C(=O)NRR', biaryl or aryl, in which

aryl is optionally substituted by -CN, halogen, aryl, alkyl, -O-alkyl, -alkyl-C(=O)O-alkyl, -alkylCOOH, -O-alkylaryl or heterocycloalkyl.

6. Use according to any one of the preceding claims, for which R1 represents alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, alkylaryl, aryl or heteroaryl, which are optionally substituted, as defined in any one of the preceding claims.

7. Use according to any one of the preceding claims, for which R1 represents alkyl or alkenyl, optionally substituted as defined in any one of the preceding claims.

8. Use according to any one of the preceding claims, for which R1 represents alkyl, optionally and independently substituted by one or more groups chosen from: -CN, aryl, heterocycloalkyl, biaryl, halogen, -C(=O)-aryl, -O-aryl, -C(=O)-alkyl, cycloalkyl, -C(=O)-alkyl, -COOH, -O-heteroaryl, -C(=O)NRR', -C(=O)-cycloalkyl, -O-heterocycloalkyl;

in which

aryl is optionally and independently substituted by one or more halogen, -CN, -O-alkylaryl, aryl, alkyl, -O-alkyl, heterocycloalkyl, -alkyl-C(=O)-OH or -alkyl-C(=O)O-alkyl;

heteroaryl is optionally substituted by heterocycloalkyl, halogen or -COOH.

heterocycloalkyl is optionally and independently substituted by one or more groups chosen from =O and alkyl.

25

9. Use according to any one of the preceding claims, for which R1 represents alkyl or alkenyl, in which the carbon α to the oxygen atom is substituted by -COOH, -C(=O)-alkyl, -C(=O)-aryl, -C(=O)-cycloalkyl, -C(=O)O-alkyl or -C(=O)NRR',

30 in which alkyl and aryl are optionally substituted as in any one of the preceding claims, and RR' are defined as in any one of the preceding claims.

10. Use according to any one of the preceding claims, for which R1 represents alkyl or alkenyl, each optionally substituted by one or more substituents chosen from halogen, -O-heteroaryl or -C(=O)-aryl, in which aryl is optionally substituted by one or more -O-alkyl and heteroaryl is optionally substituted by
5 one or more -COOH or halogen.

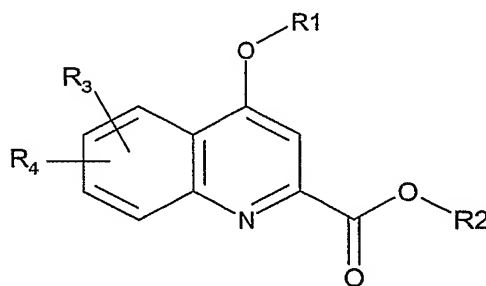
11. Use according to any one of the preceding claims, for which R2 represents a hydrogen atom or an alkyl group.

10 12. Use according to any one of the preceding claims, for which R2 represents a methyl radical.

13. Use according to any one of the preceding claims, for which R and R' represent a hydrogen atom or a methyl or ethyl radical.

15

14. Use according to any one of the preceding claims, for which the compounds of the formula (I) are represented by the general formula (II) below:



(II)

20

in which R1 and R2 are as defined in any one of the preceding claims ;

R3 and R4, which may be identical or different, independently represent groups chosen from alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, alkylaryl, heteroaryl, -CN, halogen, -O-aryl, -O-heteroaryl, cycloalkyl, heterocyclyl, -CO₂H,
25 -C(=O)-alkyl, -C(=O)-aryl, -C(=O)-cycloalkyl, -C(=O)O-alkyl, -C(=O)NRR', -OH, -O-alkyl, -O-alkylaryl, -C(=O)O-aryl, -NRR' and -S(O)_pR, in which p represents 0, 1 or 2; or

R3 and R4 may together also form a heterocycle adjacent to the phenyl ring

and also the tautomeric forms, enantiomers, diastereoisomers and epimers, and the pharmaceutically acceptable salts.

15 15. Use according to Claim 14, for which R3 and R4 represent H, -O-alkyl and/or a halogen atom or R3 and R4 together form a heterocycle adjacent to the phenyl ring.

16. Use according to Claim 14 or 15, for which R3 and R4 represent the ring -O-(CH₂)_n-O-, n being an integer ranging from 1 to 4.

10

17. Use according to any one of Claims 15 to 17, for which R3 and R4 represent, respectively, a fluorine atom in position 6 and a hydrogen atom.

18. Use according to any one of the preceding claims, for which the compounds of the general formula (I) are chosen from:

15 methyl 4-(1,3-benzothiazol-2-ylmethoxy)-6-fluoroquinoline-2-carboxylate
 methyl 4-[(4-bromo-2-fluorobenzyl)oxy]-6-fluoroquinoline-2-carboxylate
 methyl 4-ethoxy-6-fluoroquinoline-2-carboxylate
 methyl 4-[(4-bromo-2-fluorobenzyl)oxy]-6-methoxyquinoline-2-carboxylate
20 methyl 6-fluoro-4-[(3-methylbut-2-en-1-yl)oxy]quinoline-2-carboxylate
 methyl 4-[(2'-cyanobiphenyl-4-yl)methoxy]-6-fluoroquinoline-2-carboxylate
 methyl 4-(cyanomethoxy)-6-fluoroquinoline-2-carboxylate
 methyl 4-(2-chloroethoxy)-6-fluoroquinoline-2-carboxylate
 methyl 4-(2-amino-2-oxoethoxy)-6-fluoroquinoline-2-carboxylate
25 methyl 4-(allyloxy)-6-fluoroquinoline-2-carboxylate
 methyl 6-fluoro-4-(pentyloxy)quinoline-2-carboxylate
 methyl 4-[2-(4-chlorophenyl)-2-oxoethoxy]-6-fluoroquinoline-2-carboxylate
 methyl 6-fluoro-4-(2-oxo-2-phenylethoxy)quinoline-2-carboxylate
 methyl 6-fluoro-4-[2-(4-fluorophenoxy)ethoxy]quinoline-2-carboxylate
30 methyl 6-fluoro-4-(2-phenylethoxy)quinoline-2-carboxylate
 methyl 6-fluoro-4-(2-phenoxyethoxy)quinoline-2-carboxylate
 methyl 6-fluoro-4-(3-phenylpropoxy)quinoline-2-carboxylate
 methyl 4-(2-biphenyl-4-yl-2-oxoethoxy)-6-fluoroquinoline-2-carboxylate
 methyl 6-fluoro-4-[2-(4-methylphenyl)-2-oxoethoxy]quinoline-2-carboxylate

- methyl 6-fluoro-4-[2-(4-methoxyphenyl)-2-oxoethoxy]quinoline-2-carboxylate
methyl 4-[2-(1-adamantyl)-2-oxoethoxy]-6-fluoroquinoline-2-carboxylate
methyl 6-fluoro-4-[2-(4-fluorophenyl)-2-oxoethoxy]quinoline-2-carboxylate
methyl 4-[2-(3,4-dichlorophenyl)-2-oxoethoxy]-6-fluoroquinoline-2-carboxylate
5 methyl 6-fluoro-4-[2-(3-methoxyphenyl)-2-oxoethoxy]quinoline-2-carboxylate
methyl 4-[4-(4-chlorophenoxy)butoxy]-6-fluoroquinoline-2-carboxylate
methyl 6-fluoro-4-[2-(3-fluorophenoxy)ethoxy]quinoline-2-carboxylate
methyl 4-[2-(4-bromophenoxy)ethoxy]-6-fluoroquinoline-2-carboxylate
methyl 6-fluoro-4-[[5-(4-fluorophenoxy)pentyl]oxy]quinoline-2-carboxylate
10 methyl 4-[2-(4-cyanophenoxy)ethoxy]-6-fluoroquinoline-2-carboxylate
methyl 6-fluoro-4-{2-[(4-morpholin-4-yl)-1,2,5-thiadiazol-3-yl]oxy}ethoxy}quinoline-2-carboxylate
methyl 6-fluoro-4-{2-[4-(3-methoxy-3-oxopropyl)phenoxy]ethoxy}quinoline-2-carboxylate
15 methyl 6-fluoro-4-[2-(1-naphthyloxy)ethoxy]quinoline-2-carboxylate
methyl 6-fluoro-4-[2-(2-methoxyphenoxy)ethoxy]quinoline-2-carboxylate
methyl 4-{2-[2-(benzyloxy)phenyl]-2-oxoethoxy}-6-fluoroquinoline-2-carboxylate
methyl 6-fluoro-4-[2-(2-naphthyloxy)ethoxy]quinoline-2-carboxylate
methyl 4-[2-(1,3-dioxo-1,3-dihydro-2*H*-isoindol-2-yl)ethoxy]-6-fluoroquinoline-2-
20 carboxylate
methyl 4-[1-(ethoxycarbonyl)-3-phenylpropoxy]-6-fluoroquinoline-2-carboxylate
methyl 4-[2-(2,3-dimethylphenoxy)ethoxy]-6-fluoroquinoline-2-carboxylate
methyl 6-fluoro-4-{2-[4-(2-methyl-1,3-dioxolan-2-yl)phenyl]ethoxy}quinoline-2-carboxylate
25 methyl 4-{2-[4-(benzyloxy)phenyl]-2-oxoethoxy}-6-fluoroquinoline-2-carboxylate
methyl 4-[2-(3,4-dimethoxyphenyl)-2-oxoethoxy]-6-fluoroquinoline-2-carboxylate
methyl 4-(3-chloropropoxy)-6-fluoroquinoline-2-carboxylate
methyl 4-(3-chloro-2-methylpropoxy)-6-fluoroquinoline-2-carboxylate
methyl 4-(1-ethylpropoxy)-6-fluoroquinoline-2-carboxylate
30 methyl 6-fluoro-4-[(1-methylhexyl)oxy]quinoline-2-carboxylate
methyl 4-[2-(2,4-dimethoxyphenyl)-2-oxoethoxy]-6-fluoroquinoline-2-carboxylate
methyl 4-(3,3-dimethyl-2-oxobutoxy)-6-fluoroquinoline-2-carboxylate
methyl 6-fluoro-4-(3-phenoxypropoxy)quinoline-2-carboxylate
methyl 4-[(4-bromo-2-fluorobenzyl)oxy]-6-fluoroquinoline-2-carboxylic acid

- methyl 4-(1,3-benzothiazol-2-ylmethoxy)-6-fluoroquinoline-2-carboxylic acid
4-ethoxy-6-fluoroquinoline-2-carboxylic acid
4,4'-[(2E)-but-2-ene-1,4-diylbis(oxy)]bis(6-fluoroquinoline-2-carboxylic acid)
6-fluoro-4-[(3-methylbut-2-en-1-yl)oxy]quinoline-2-carboxylic acid
5 4-[(2'-cyanobiphenyl-4-yl)methoxy]-6-fluoroquinoline-2-carboxylic acid
sodium 4-[(4-bromo-2-fluorobenzyl)oxy]-6-methoxyquinoline-2-carboxylate
4-(cyanomethoxy)-6-fluoroquinoline-2-carboxylic acid
4-(2-chloroethoxy)-6-fluoroquinoline-2-carboxylic acid
4-(2-amino-2-oxoethoxy)-6-fluoroquinoline-2-carboxylic acid
10 4-(allyloxy)-6-fluoroquinoline-2-carboxylic acid
4-(3-chloropropoxy)-6-fluoroquinoline-2-carboxylic acid
4-(3-chloro-2-methylpropoxy)-6-fluoroquinoline-2-carboxylic acid
6-fluoro-4-(pentyloxy)quinoline-2-carboxylic acid
4-(cyclohexylmethoxy)-6-fluoroquinoline-2-carboxylic acid
15 6-fluoro-4-[2-(4-fluorophenoxy)ethoxy]quinoline-2-carboxylic acid
6-fluoro-4-(2-phenylethoxy)quinoline-2-carboxylic acid
6-fluoro-4-(3-phenylpropoxy)quinoline-2-carboxylic acid
4-[2-(1-adamantyl)-2-oxoethoxy]-6-fluoroquinoline-2-carboxylic acid
6-fluoro-4-[2-(4-fluorophenyl)-2-oxoethoxy]quinoline-2-carboxylic acid
20 6-fluoro-4-[2-(3-methoxyphenyl)-2-oxoethoxy]quinoline-2-carboxylic acid
4-[4-(4-chlorophenoxy)butoxy]-6-fluoroquinoline-2-carboxylic acid
6-fluoro-4-[2-(3-fluorophenoxy)ethoxy]quinoline-2-carboxylic acid
4-[2-(4-bromophenoxy)ethoxy]-6-fluoroquinoline-2-carboxylic acid
6-fluoro-4-[[5-(4-fluorophenoxy)pentyl]oxy]quinoline-2-carboxylic acid
25 4-[2-(4-cyanophenoxy)ethoxy]-6-fluoroquinoline-2-carboxylic acid
6-fluoro-4-{2-[(4-morpholin-4-yl)-1,2,5-thiadiazol-3-yl]oxy}ethoxy}quinoline-2-carboxylic acid
4-{2-[4-(2-carboxyethyl)phenoxy]ethoxy}-6-fluoroquinoline-2-carboxylic acid
6-fluoro-4-[2-(2-methoxyphenoxy)ethoxy]quinoline-2-carboxylic acid
30 4-(1-carboxy-3-phenylpropoxy)-6-fluoroquinoline-2-carboxylic acid
4-[2-(2,3-dimethylphenoxy)ethoxy]-6-fluoroquinoline-2-carboxylic acid
4-[2-(3,4-dimethoxyphenyl)-2-oxoethoxy]-6-fluoroquinoline-2-carboxylic acid

and also the tautomeric forms, enantiomers, diastereoisomers and epimers, and the pharmaceutically acceptable salts.

19. Use according to any one of the preceding claims, for which the compounds of the general formula (I) are chosen from:

- 4-(4-bromo-2-fluorobenzyloxy)-6-fluoroquinoline-2-carboxylic acid
- 4-(benzothiazol-2-ylmethoxy)-6-fluoroquinoline-2-carboxylic acid
- 4-ethoxy-6-fluoroquinoline-2-carboxylic acid
- 4-(4-bromo-2-fluorobenzyloxy)-6-methoxyquinoline-2-carboxylic acid
(sodium salt)
- 4-({(E)-4-[(2-carboxy-6-fluoro-4-quinolinyl)oxy]-2-butenyl}oxy)-6-fluoroquinoline-2-carboxylic acid
- 6-fluoro-4-(3-methylbut-2-enyloxy)quinoline-2-carboxylic acid
- 4-(2'-cyanobiphenyl-4-ylmethoxy)-6-fluoroquinoline-2-carboxylic acid
- 4-[2-(3,4-dimethoxyphenyl)-2-oxo-ethoxy]-6-fluoroquinoline-2-carboxylic acid
- methyl 4-(3-chloropropoxy)-6-fluoroquinoline-2-carboxylate
- methyl 4-(3-chloro-2-methylpropoxy)-6-fluoroquinoline-2-carboxylate

and also the tautomeric forms, enantiomers, diastereoisomers and epimers, and the pharmaceutically acceptable salts.

20. Use according to any one of the preceding claims, for which the said pharmaceutical composition is suitable for the treatment of diabetes.

21. Use according to any one of the preceding claims, for which the said pharmaceutical composition is suitable for the treatment of type II diabetes.

22. Use according to any one of the preceding claims, for which the pharmaceutical composition is suitable for the treatment of diseases chosen from dyslipidaemia and obesity.

23. Use according to any one of the preceding claims, for which the pharmaceutical composition is suitable for the treatment of diseases chosen from diabetes-related microvascular and macrovascular complications.

24. Use according to any one of the preceding claims, for which the said complications include arterial hypertension, atherosclerosis, inflammatory processes, microangiopathy, macroangiopathy, retinopathy and neuropathy.

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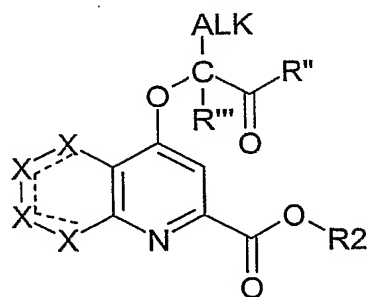
25. Use according to any one of the preceding claims, for which the pharmaceutical composition is suitable for reducing hyperglycaemia.

26. Compounds of the general formula (I) as defined in any one of the preceding claims, for which

R1 represents alkyl in which the carbon α to the oxygen atom is substituted by -COOH, -C(=O)-alkyl, -C(=O)-aryl, -C(=O)-cycloalkyl, -C(=O)O-alkyl or -C(=O)NRR', in which alkyl and/or aryl are optionally substituted as defined in any one of the preceding claims,

15 and also the tautomeric forms, enantiomers, diastereoisomers and epimers, and the pharmaceutically acceptable salts.

27. Compounds according to Claim 26 represented by the general formula (III):



(III)

20

in which

X, R₂, R, R' and  are as defined in any one of the preceding claims,

ALK represents an alkyl or alkenyl radical optionally substituted by one or more of the following groups: -CN, halogen, aryl, biaryl, -O-aryl, -O-heteroaryl, -O-heterocycloalkyl, cycloalkyl, heterocycloalkyl, -CO₂H, -C(=O)-alkyl, -C(=O)-aryl, -C(=O)-cycloalkyl, -C(=O)O-alkyl, -C(=O)NRR', -OH, -O-alkyl, -O-alkylaryl, -C(=O)O-aryl, -NRR', -S(O)_pR, in which p represents 0, 1 or 2;

25

R'' is chosen from -OH, alkyl, aryl, cycloalkyl, -O-alkyl and -NRR', in which:

alkyl is optionally substituted by one or more of the following groups: -CN, halogen, aryl, biaryl, -O-aryl, -O-heteroaryl, -O-heterocycloalkyl, cycloalkyl, heterocycloalkyl, -CO₂H, -C(=O)-alkyl, -C(=O)-aryl, -C(=O)-cycloalkyl, -C(=O)O-alkyl, -C(=O)NRR', -OH, -O-alkyl, -O-alkylaryl, -C(=O)O-aryl, -NRR', -S(O)_pR, in which p represents 0, 1 or 2;

aryl is optionally substituted by one or more groups chosen from: -CN, halogen, aryl, alkyl, -O-alkyl, -alkyl-C(=O)O-alkyl, -alkyl-C(=O)OH, -O-alkylaryl, heterocycloalkyl, -NRR', -OH, -S(O)_pR, in which p represents 0, 1 or 2; -O-aryl, perhaloalkyl, -COOH, COOR;

heteroaryl is optionally and independently substituted by one or more groups chosen from halogen, -COOH and heterocycloalkyl;

heterocycloalkyl is optionally and independently substituted by one or more alkyl or = O;

R''' is H, alkyl or alkenyl optionally substituted by one or more of the following groups: -CN, halogen, aryl, biaryl, -O-aryl, -O-heteroaryl, -O-heterocycloalkyl, cycloalkyl, heterocycloalkyl, -CO₂H, -C(=O)-alkyl, -C(=O)-aryl, -C(=O)-cycloalkyl, -C(=O)O-alkyl, -C(=O)NRR', -OH, -O-alkyl, -O-alkylaryl, -C(=O)O-aryl, -NRR', -S(O)_pR, in which p represents 0, 1 or 2;

and also the tautomeric forms, enantiomers, diastereoisomers and epimers, and the pharmaceutically acceptable salts.

28. Compounds according to Claim 26 or 27, for which

R'' represents -OH, alkyl, aryl, cycloalkyl, -O-alkyl or -NRR', in which aryl is optionally substituted by -O-alkylaryl, -O-alkyl, alkyl, aryl or halogen; ALK represents alkyl optionally substituted by aryl;

R''' represents H;

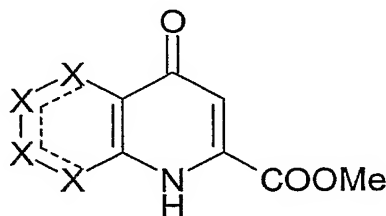
X each represent a carbon atom, optionally substituted by a halogen atom,


R₂ represents H or an alkyl radical,

R and R' represent a hydrogen atom or an alkyl radical.

29. Compounds according to any one of Claims 26 to 28, for which X represents a carbon atom optionally substituted in position 6 of the quinoline ring system with a fluorine atom.

- 5 30. Process for the preparation of the compounds of the formula (I) or (III) defined according to any one of Claims 26 to 29, comprising the step consisting in reacting compound (3):



- 10 in which X and  are as defined in any one of the preceding claims, with a compound of the formula R1-Hal, in which Hal represents a halogen atom, and R1 is as defined in any one of Claims 26 to 29, in a suitable organic solvent, in alkaline medium, at a temperature of between room temperature and the boiling point of the solvent, and optionally the step consisting in saponifying the
- 15 product obtained, in an alcoholic solvent, in the presence of a base, optionally followed by the step consisting in esterifying the product obtained with a corresponding alcohol of the formula R2-OH, in which R2 is as defined in any one of the preceding claims, in an alcoholic solvent, in acidic medium.

- 20 31. Process according to Claim 30, comprising the step consisting in isolating the product obtained.

32. Pharmaceutical compositions comprising, as active ingredient, at least one derivative of the general formula I or III as defined in any one of Claims 26 to
- 25 29.